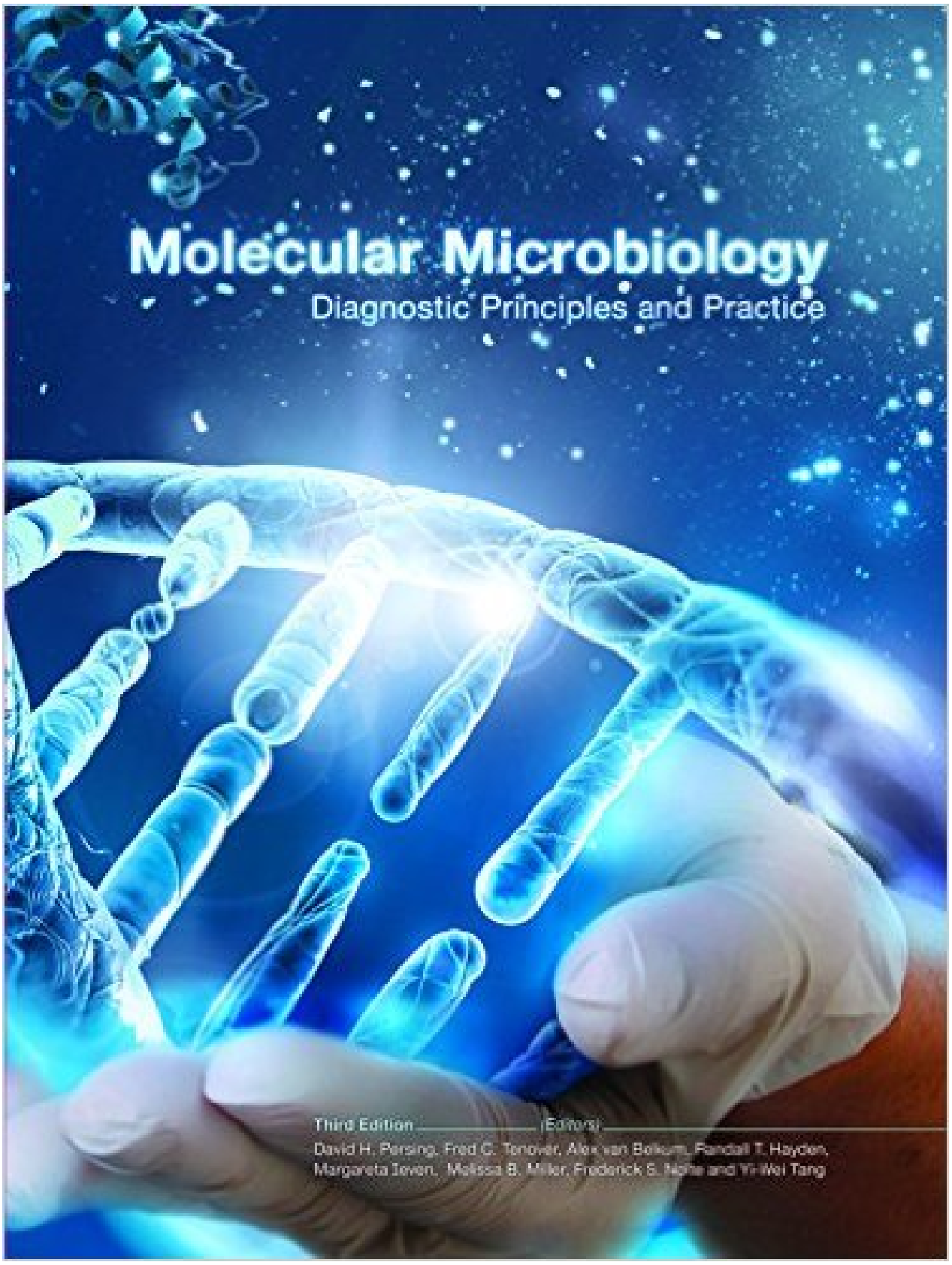
Molecular Microbiology
Diagnostic Principles and Practice
Third Edition
Editor(s):
David H. Persing, Fred C. Tenover, Alex van Belkum, Randall T. Hayden,
Margareta Ieven, Melissa B. Miller, Frederick S. Nolte and Yi-Wei Tang

Using Nucleic Acid Amplification Techniques in a Syndrome-Oriented Approach: Detection of Respiratory Agents. K. Loens and M. Ieven. In: Molecular Microbiology. Diagnostic Principles and Practice. Third Edition. D. H. Persing, F. C. Tenover, R. T. Hayden, M. Ieven, M. B. Miller, F. S. Nolte, Y-W Tang, and A. van Belkum. ASM Press. 2016. p306-335.

Abstract:

Lower respiratory tract infections (LRTI) are an important problem. They occur frequently, are associated with significant morbidity and mortality, are present in a variety of healthcare settings and impose a considerable cost to European healthcare services.

In developed countries, while mortality has declined spectacularly during the twentieth century, LRTIs remain a leading cause of death. WHO statistics estimate that mortality from respiratory infections is 48/100 000 worldwide and ranges from 40 to 50/100 000 in Europe (WHO's 2002 annual report at http://www.who.org/).

Such figures stress the importance of early recognition of those patients who are severely ill or at risk of becoming severely ill. Of all RTIs about one third are thought to involve the lower respiratory tract, with +/- 10% community acquired pneumonia (CAP), the remaining two thirds affecting the upper respiratory tract.

At present there is still a great deficit in the etiologic diagnosis of community-acquired lower respiratory tract infections (LRTI): in most studies more than 50% of cases remain without an etiologic diagnosis resulting in unnecessary or inappropriate antibiotic prescribing.

A wide variety of diagnostic procedures and techniques are applied for the detection of the etiologic pathogens of community-acquired LRTI. Traditional diagnostic culture methods above all lack sensitivity, are not feasible in many contexts, and focus only on a few of the large number of etiologic agents. For example, for years, viruses were rarely thought of as the etiologic agent of LRTIs except for cases involving children and immunocompromised patients. However, it has been demonstrated that viruses, in particular RNA viruses, may cause LTRIs and even pneumonia in otherwise healthy adults. Multiple pathogen infections are also more and more detected (1).

For the so called "atypical" bacterial causes *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae* and *Legionella pneumophila*, traditional diagnostic methods are also too insensitive and too slow, producing a result only after several days.

Therefore alternative diagnostic procedures were developed: antigen detection by latex agglutination or immunofluorescence (DIF), ELISA, immunochromatography and nucleic acid amplification techniques (NAATs), particularly PCR and NASBA (nucleic acid sequence-based amplification).

Over the past two decades, NAATs are revolutionizing the diagnostic procedures for the management of patients with LRTI, resulting from a combination of improved sensitivity and specificity, a potential for automatization and the production of very rapid results. NAATs have already become the gold-standard in some diagnostic fields, however, not many assays have been approved by the US Food and Drug Administration for the detection of respiratory pathogens and fewer still have entered the daily routine diagnosis and management of patients. This can be ascribed to the rapid evolution of the technology, the cost of this technology and the large number of etiological agents, bacterial as well as viral, responsible for community-acquired LRTI.

This overview will therefore provide a look at the general principles, advantages, diagnostic value, and limitations of the most currently used new amplification techniques for the etiological diagnosis of respiratory tract infections as they evolve from research to daily practice.